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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,785	02/15/2002	Saverio Carl Falco	BB1336 USCNT	4051

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EXAMINER	
KERR, KATHLEEN M	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 03/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/076,785	FALCO ET AL.	
	Examiner	Art Unit	
	Kathleen M Kerr	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application Status

1. In response to the previous Office action, a written restriction requirement (mailed on November 28, 2003), Applicants filed a response and amendment received on December 22, 2003 and January 15, 2004 (to correct the format of the proposed amendment). Said amendment cancelled Claims 1-30 and added new Claims 31-43. Thus, Claims 31-43 are pending in the instant Office action.

Election

2. Applicants' election without traverse of Group VI in a paper received on December 22, 2003 is acknowledged. The new Claims 31-43 are drawn to the elected invention. Thus, Claims 31-43 will be examined herein.

Priority

3. The instant application is granted the benefit of priority for the U.S. Provisional Application No. 60/119,599 filed on February 10, 1999 and for the U.S. non-provisional Application No. 09/501,423 filed on February 9, 2000 as requested in the declaration and/or the first lines of the specification.

The Examiner notes that SEQ ID NOs:23/24 (full length sequences) are not taught by the provisional application.

Information Disclosure Statement

4. The information disclosure statement filed on February 15, 2002 has been reviewed, and its references have been considered as shown by the Examiner's initials next to each citation on the attached copy.

Sequence Compliance

5. The updated sequence listing filed on December 22, 2003 has been entered.

Objections to the Specification

6. The specification is objected to because the title is not descriptive. A new title is required that is clearly indicative of the invention to which the elected claims are drawn (see M.P.E.P. § 606.01). The Examiner suggests the following new title:

---Polynucleotides Encoding Plant Cysteine Proteases---

7. The specification is objected to for being unclear as to the nature of subclasses of cysteine proteases described therein. A general discussion of cysteine proteases is found in the introduction on pages 1-2; EP-A and EP-B subclasses are noted in barley. Table 1 on pages 5-6 identifies calpain 94 and CLP proteases, which subclasses of proteases are well known in the art and are described in references cited in pages 1-2 of the instant specification. However, cysteine proteases 1 and 2, while identified in Table 1, are not described as named subclasses in the references cited on pages 1-2.

While it is clear that these names were defined by homologies to GI:1706260 (for cysteine protease 1) and GI:2511691 (for cysteine protease 2) (see Examples 4-5 in the

specification), this prior art is does not identify these as known subclasses. As related to GI:1706260, two cysteine proteases were found in corn (Domoto *et al.*) (they are named 1 and 2 arbitrarily), and Applicants' wheat and rice sequences are related to this "1"; but since only one cysteine protease sequence is found by Applicants in each of wheat and rice, the numbering of "1" is unclear. As related to GI:2511691, two cysteine proteases were found in kidney bean (Becker *et al.*) (they are named 1 and 2 arbitrarily), and Applicants' soybean sequence is related to this "2"; but since only one cysteine protease sequence is found in soybean by Applicants, the numbering of "2" is unclear. Clarification on this numbering system is required. Alternatively, the Examiner suggests removal of the numbers related to cysteine proteases.

8. The amendment filed February 15, 2002 (the filing date of the instant application) is objected to under 35 U.S.C. § 132, new matter, because it introduces new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention. Although the amendment was filed on the filing date of the instant application, said amendment is not referred to in the declaration and is, thus, considered an amendment and not an original part of the specification (see M.P.E.P. § 608.04(b)). The added material which is not supported by the original disclosure is as follows:

a) Incorporating the priority documents by reference in the first paragraph of the specification, unless the entire disclosure of the priority documents, as amended if applicable, can be supported by the filing of the instant application.
b) All amendments to the sequences iterated in the specification (but not the claims) since these changes alter the definition of the SEQ ID NOs (for example, on page 2, line 13, SEQ ID NO:8 would now be identified as a calpain 94 polypeptide wherein the originally filed document it was not).

The Examiner has carefully considered Applicants' explanation for the amendments and how it is believed that they are supported in the specification as originally filed. However, the Examiner disagrees that such amendments were supported in the application as originally filed.

With respect to item (i) in each case, the fact that the original filing describes rice sequences as 7 and 8 (which are contradictorily corn sequences in the sequence listing as originally filed) merely indicates an inconsistency and does not indicate sequences 13 and 14 as the rightful sequences in that position in the Table 1, for example, particularly because 13 and 14 are *not* the only rice sequences disclosed. With respect to item (ii), it is clear that Table 6 describes rr1.pk084.j16 as being related to a cysteine protease 1; however, rr1.pk084.j16 is not clearly identified as SEQ ID NO:13 since rr1.pk084.j16 is disclosed as SEQ ID NO:7 in Table 1 as originally filed. While the Examiner does not disagree that SEQ ID NO:7 could not be mistaken for a cysteine protease by one of skill in the art upon an in-depth investigation into sequence homologies, the % identity error referred to in item (iii) is not **readily apparent** in the original disclosure. The standard for new matter is found in M.P.E.P. § 608.04(a):

> "Matter not in the original specification, claims, or drawings is usually new matter. Depending on circumstances such as the adequacy of the original disclosure, the addition of inherent characteristics such as chemical or physical properties, a new structural formula or a new use may be new matter."

While the Examiner agrees that these were probably oversight-type errors on the part of Applicants, which does not change the fact that SEQ ID NO:13 was not identified as a cysteine protease 1 gene, for example, in the original disclosure.

Since the changes above were filed in a preliminary amendment on the day of filing, if Applicants file a substitute declaration citing the understanding of said preliminary amendment,

signed by all the inventors, the preliminary amendment filed on the day of filing can be considered part of the original disclosure. In this case, Applicants would also be required to change the status of the instant application to a continuation-in-part of the parent case, 09/501,423 since the instant case would no longer be an exact copy of the parent case.

The Examiner notes that the amendments to the claims in the preliminary amendment filed February 15, 2002 do *not* constitute new matter because the specification notes, on page 9, all polynucleotides disclosed in the specification as having the breadth noted in the amended claims; no definitions of the functionality of the SEQ ID NOs have been altered in this amendment.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 31-43 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claims 31-36, the phrase "compared to one of SEQ ID NO:24" is confusing since only one sequence is listed. Clarification is required.

10. Claims 38, 40 and 42-43 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 38, a recombinant DNA construct is required, but its recombinant nature is unclear since naturally occurring cysteine proteases are known to be linked

to homologous regulatory sequences in nature. To be clear, the Examiner suggests rewriting the claim as requiring ---a heterologous regulatory sequence---.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 31-34 and 37-43 are rejected under 35 U.S.C. § 112, first paragraph, scope of enablement, because the specification, while being enabling for polynucleotides which encode SEQ ID NO:24, does not reasonably provide enablement for polynucleotides with such low sequence identity, such as the 80% identity claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The amount of experimentation required of one of skill in the art to use the claimed invention to the full extent of its scope is undue.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by

weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a prima facie case is discussed below.

The instant specification describes one cysteine protease 2 from the art, GI:2511691 from *Phaseolus vulgaris* and discloses one new protein soybean (see Example 5). No general disclosure of the structure of cysteine protease 2 enzymes (or cysteine proteases in general) is found, particularly a discussion of structure as it relates to function is absent. Applicants present no guidance or working examples of the use of polynucleotides that have such low sequence identity with respect to SEQ ID NO:24. The nature of the invention is such that the DNA encodes a functional protein, a cysteine protease 2; and with such a great deviation from the known sequence, the predictability of functionality becomes extremely low. The art fully enables any DNA encoding SEQ ID NO:24 based on the degeneracy of the genetic code. While the instant specification describes and enables means for identifying other cysteine protease 2 genes related to SEQ ID NO:23 using hybridization methods, etc., these methods do not enable one of skill in the art to make all, or a relevant portion of, the polynucleotides within the scope of the claims because the ability to find a cysteine protease 2 gene, which is structurally related to SEQ ID NO:23, is not equivalent to the ability to make a cysteine protease 2 gene as required by the statute (i.e., "make and use"). No description in the specification or the

art provides particular residues whose encoding is important within the disclosed sequence so that its cysteine protease 2-nature is maintained. Thus, one of skill in the art would be unable to predict the structure of the other members of the genus in order to make such members. Therefore, the instant claims are not enabled to the full extent of their scope without undue experimentation.

12. Claims 31-43 are rejected under 35 U.S.C. § 112, first paragraph, new matter, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The new matter is as follows:

a) in Claim 31, the identification of SEQ ID NO:24 as a cysteine protease, and

b) in Claim 37, the term "recombinant".

In support of Claim 31, Applicants are relying on the introduction of the preliminary amendment filed on February 15, 2002, which is noted above as introducing new matter.

In support for Claim 38 drawn to a recombinant DNA construct, Applicants note page 13, line 26. This portion of the specification refers generally to recombinant DNA techniques and does not clearly support product claims to recombinant DNA constructs containing regulatory sequences.

Applicants are required to cancel the new matter in response to the instant Office action or to cite clear support, page and line number, for the amendments.

Closest Prior Art

13. The Examiner notes the following as being the closest prior art to the structure of the pending product claims:

a) Becket *et al.* (see IDS) teach a gene encoding a cysteine protease from *Phaseolus vulgaris* that encodes a protein that is 78% identical (87% similar) to SEQ ID NO:24. Thus, Claims 31-43 are considered free of the prior art. The Examiner also notes that while no particular utility for the claimed invention is described in the specification, utility of cysteine proteases is well-known in the art for use in protein degradation, such as in laundry detergents.

Other Noteworthy Art

14. The following are citations of related prior art that do not read on the pending claims for the reasons noted:

a) Nong *et al.* (cDNA cloning for a putative cysteine proteinase from developing seeds of soybean. Biochimica et Biophysica Acta (1995) 1261:435-438) teach a cysteine proteinase from soybean whose amino acid sequence is about 40% identical to SEQ ID NO:24 (see attached alignment). It is not uncommon for two putative cysteine proteinases in the same plant to be this dissimilar (see Becker *et al.* –IDS -with sequences only 32% identical and Domoto *et al.* – IDS –with sequences only 42% identical).
b) Asano *et al.* (Characterization of novel cysteine proteases from germinating cotyledons of soybean [Glycine max (L.) Merrill]. Journal of Biochemistry (1999) 126(2):296-301) teach two cysteine proteases purified from soybean of 26,178 and 26,429 Da; no protein *sequences* are disclosed. The sizes of these mature proteins are consistent with neither the protein of Nong *et al.* (mature protein postulated as 26,355 Da) nor SEQ ID NO:24 (mature form not postulated).

Conclusion

15. Claims 31-43 are not allowed for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kathleen M Kerr whose telephone number is (571) 272-0931. The examiner can normally be reached on Monday through Friday, from 9:00am to 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathupura Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Kathleen M Kerr
Examiner
Art Unit 1652

March 4, 2004